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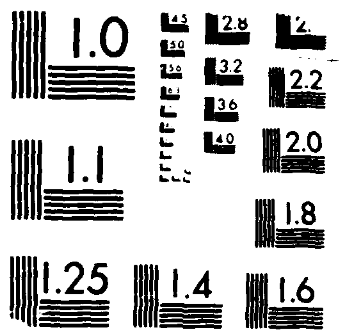

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A new method has been developed to characterize the sources of spontaneous brain activity measured magnetically while avoiding any specific model for the neural generators. In an application of the technique, individual spindles of the alpha rhythm monitored by a set of 14 magnetic sensors fixed over the occipital lobe were characterized as vectors in a 14-dimensional signal space. Taking the noise level into account, the number of distinct vectors could be determined, which indicates the number of sources that differ in their geometrical attributes such as position, orientation, and extent. In a pilot study of about 30 spindles for each of two subjects, virtually all sources were distinguishable from the others, implying a large set of underlying generators.

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NEW METHOD FOR THE STUDY OF SPONTANEOUS BRAIN ACTIVITY

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INTRODUCTION

We have developed new methods to analyze multichannel neuromagnetic recordings of spontaneous brain activity that avoid specific assumptions concerning the nature of the sources. This approach can be applied to studies of a variety of brain signals, such as alpha rhythm and interictal epileptic activity, for the purposes of classification and analysis, even if the field pattern over the scalp may not be characterized as that of a single current dipole. We illustrate this approach by applying these methods to the study of the alpha rhythm in human subjects.

By definition (Chatrian et al., 1974), the alpha rhythm is brain activity that gives rise to electrical oscillations between 8 and 13 Hz on the occipital scalp and is attenuated by visual stimuli. The cortical origin of alpha activity has been evidenced by studies of potentials at various depths within the cortex of animals (Calvet et al. 1964; Creutzfeldt and Houchin, 1974; Frost, 1968) and especially by a clear polarity reversal between superficial and depth electrodes in dog (Lopes da Silva and van Leeuwen, 1978). These last studies also provided evidence that alpha activity originates in different epicenters from which activity spreads in several directions, rather than originating in a single source and sweeping over a large area of cortex.

Previous neuromagnetic studies (Carelli et al., 1983; Vvedensky et al., 1986) suggest that many sources responsible for magnetically monitored alpha activity are located near or in the visual cortex and there are time series of the rhythm during periods of strong activity in which the oscillation period is constant. These time series are called *spindles*. The magnetic field pattern during a spindle appears to remain relatively stable. Based on these findings, we adopt the working hypothesis that there are *specific configurations of neurons* that exhibit such oscillatory excitations. We call such oscillations *alphons*. These hypothetical oscillations would be basic units of activity, whose signals add up to form the observed alpha rhythm. Our analysis was developed to test this alphon hypothesis by determining whether the underlying sources of spindles can be said to differ significantly. In particular it would be interesting to determine whether an alphon can be associated with many spindles, indicating that the alphon exhibited repeated oscillations.

It is possible to characterize the source configuration of an alphon without the use of any model, such as a current dipole model. We study the kinematics of the alpha rhythm in an n-dimensional "signal" space, as defined by the output amplitudes of the n-sensor system. The lead fields of n detection coils are not generally orthogonal in current space (Hämäläinen and Ilmoniemi, 1984) nor do they form a complete set of basis vectors (they span a subspace of the current space). Nevertheless, even without orthogonalizing the set of n basis vectors we may investigate the distribution of activity within this space. A given source configuration corresponds to a specific direction for its *spindle vector* in signal space, as defined by the 14 sensor outputs, and a greater distance from the origin in a fixed direction represents greater source strength. Thus we may ignore source strength *per se* in our discussion if we confine consideration to direction alone. For instance, we can determine whether more than one spindle can be attributed to the same alphon by establishing whether the spindle vector in this space points in the same direction as the spindle from that alphon (the *alphon vector*). Furthermore, it would be possible to determine whether different directions of signal space have characteristic features, such as different alpha frequencies.

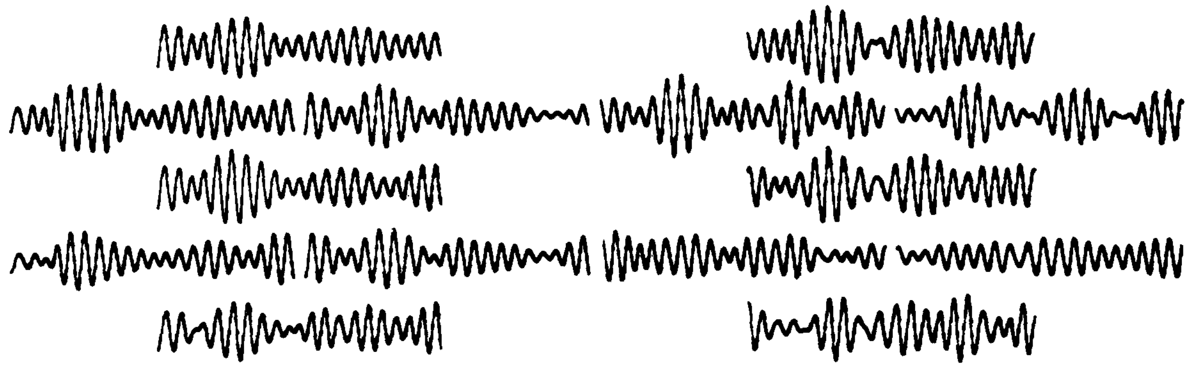


Fig. 1. Observed 2-second time series from subject RJI within the bandwidth from 8 to 13 Hz showing alpha activity. The array of recordings indicates the relationship of the 7 detection coils within an individual probe, but the relative orientation of one probe to another is not correctly indicated.

METHODS

Alpha activity for two subjects was recorded with the GEMINI system at the Center for Neuromagnetism of the New York University Medical Center. This system has two probes in separate dewars, each with seven second-order SQUID gradiometers. When maintained in fixed positions the system defines a 14-dimensional signal space. The geometry of the detection coils within each probe is identical to that of a 5-sensor probe described by Williamson et al. (1984) except that each central detection coil is surrounded by 6 rather than 4 outrider coils, which lie on a circle 4 cm in diameter. The subject was prone on a bed in a room with subdued lighting, with an unobstructed downward view onto a patterned surface. The probes were positioned over the occipital area of the scalp about 5 cm above the inion and 6 cm to either side of the midline, where the alpha signals were found to be strongest. Data were recorded continuously for 12-second epochs, with the subject's eyes closed; and at fixed intervals recordings were done with eyes open to verify the existence of alpha blocking in this condition and to obtain an estimate of the background noise. The recording bandwidth was 1-50 Hz; for analysis, the passband was narrowed to the alpha band, i.e., 8-13 Hz.

The initial analysis of the data consists of using a computer to automatically detect intervals of strong spindles and picking those that have a stable period and no phase shifts across sensors. Typically, 1 to 5 such spindles were detected during a 12-second epoch. If the alphon hypothesis were valid, these spindles could be due to individual alphons, and the field pattern should remain stable in signal space during each spindle's lifetime. Figure 1 shows representative data for the 14 sensors. To improve the signal-to-noise ratio in determining spindle amplitudes, the covariance between the signal of a given sensor and each of the other signals was computed. These covariances were added together and divided by the sum of the other signal amplitudes to obtain the portion of the given sensor's signal that is coherent across sensors. The 14 amplitudes thus obtained define the components of the spindle vector in signal space.

To determine whether the source configuration of two spindles differ significantly, we need only determine whether the angle between their spindle vectors differs significantly from the noise. Conceptually, it may be useful to consider noise for each measurement as represented by an ellipsoid in signal space (Fig. 2a). It is an ellipsoid rather than a sphere, since generally the instrumental, environmental, and subject noise differ across sensors, and the latter two may also be correlated across sensors. If we imagine such a noise ellipsoid centered on the head of each spindle vector, then when the ellipsoids of two spindle vectors do not have angular overlap, the measurement has indicated the existence of separate source configurations.

All pairs (i,j) of spindle vectors were analyzed to determine whether their angle of separation α_{ij} significantly exceeds the noise. We determined this by projecting in turn the background noise for each of the 14 sensors onto the plane defined by the pair of spindle vectors, and adding these noise vectors to the ith spindle vector with signs for their components that most quickly bring the resultant vector toward the jth spindle vector (Fig. 2b). The corresponding angle between the ith spindle vector and the resultant when noise is added is called the *noise angle* η_{ij}. In a similar fashion the noise angle η_{ji} for the second spindle vector is

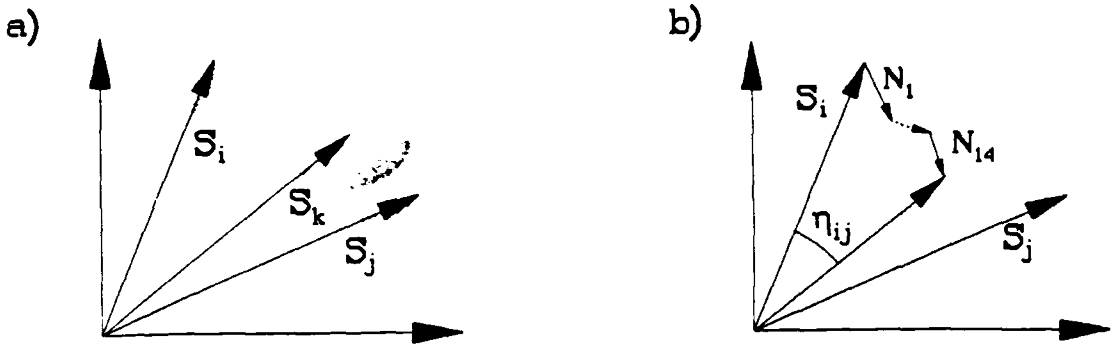


Fig. 2. (a) A representation of spindle vectors S_i, S_j, S_k and the noise ellipsoids in 14-dimensional signal space. The angle between S_i and S_j is denoted by α_{ij}. (b) Definition of the noise angle η_{ij} from S_i toward S_j, obtained by adding projected noise vectors N_1, N_2, ..., N_{14} for each of the sensors.

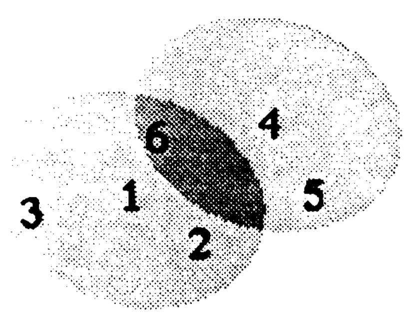
computed. The total noise angle is then taken as $\varepsilon_{ij} = [\eta_{ij}^2 + \eta_{ji}^2]^{1/2}$. We introduce the *discrimination ratio* $D_{ij} = \alpha_{ij}/\varepsilon_{ij}$ to represent the angular separation of two spindle vectors compared to the noise. D_{ij} is a measure of the significance of the difference between a pair of spindle sources. All spindles that cannot be distinguished from a given one are called its *neighbors*.

The data for 4 trials with subject RJI and 3 trials for subject FAL were analyzed as described above. Each trial contained 18 twelve-second epochs, the epochs being separated by 8 seconds. In each trial, 26 to 35 spindles were found, based on the criteria that a spindle has to exceed a minimum amplitude of 0.5 pT and a minimum duration of 500 ms, and that the oscillations in different sensors must be coherent. In addition, phase stability within each channel during a spindle was required.

RESULTS

Typical spindles had durations under 2 sec and peak-to-peak amplitudes of about 1-2 pT. The range of observed frequencies for RJI was from 10.0 to 11.2 Hz and for FAL from 9.6 to 10.8 Hz. Typical angles between spindle vectors in signal space were 10-30 deg. With our signal-to-noise ratio of about 8, we found for both subjects that almost every spindle could be distinguished from each of the others in a trial with a discrimination ratio $D_{ij} = 2.0$. Therefore, each spindle characterizes a different alphon at this discrimination level. The same was true with $D_{ij} = 4.0$ for FAL, but at this level for RJI only 9-12 alphons were needed to explain each set of 27 to 35 spindles in a trial. Using the terminology defined in Fig. 3, a typical alphon could account for 3 to 10 spindles (the *cohorts* of the alphon), and each spindle could be explained by any of 1 to 6 alphons (*candidates* for the spindle). Successive spindles were often less distinguishable from each other than spindles separated by longer times. Generally, as the signal-to-noise ratio increases so that spindles may be

Fig. 3. Illustration of spindle relationships in signal space. The neighborhood of spindle vector 1 (stipled) includes spindles 2, 3 and 6, so these three spindles are its neighbors. If spindle 1 defines an alphon, spindles 2, 3 and 6 are its cohorts. The neighborhood of spindle 4 includes spindles 5 and 6, so if spindle 4 defines an alphon these two are its cohorts. From the point of view of spindles that do not define alphons, spindles 2, 3 and 6 have alphon 1 as their candidate, and spindles 5 and 6 have alphon 4 as their candidate. Consequently, spindle 6 has two alphons (1 and 4) as candidates for its source.



better discriminated from each other, we expect to have fewer cohorts for each alphon and fewer candidates for each spindle.

Spindles that are cohorts of a given alphon were often found to have differing frequencies. Therefore, either an alphon is not limited to oscillating at a given frequency each time it is excited, or with improved signal-to-noise ratio we could be able to distinguish between these spindles of differing frequency.

CONCLUSIONS

This study shows it is possible to distinguish between most of the sources of observed spindles using the spindle vector representation. For the present subjects, some spindles that are cohorts of an alphon are found to have differing physical properties such as frequency. This implies that to within the resolution of our measurements the underlying neural excitation with fixed geometry can be modulated. Our results indicate that the alpha rhythm is generated by a large number, or possibly a continuum, of different source configurations. It remains to be seen whether most or even any of these are locally oscillating portions of cortex so that they might be modeled by current dipoles.

It has not escaped our attention that analyses of this type can be applied to classify the sources of signals from other types of neural excitations, such as interictal epileptic activity. One advantage is that this method is not computationally demanding, and model-specific analyses need be performed only once for each class, such as for an alphon representing all of its cohorts.

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